10/519518
BT01 Rec'd PCT/PTC 23 DEC 2004

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-32. (Canceled)

33. (New) A metal electrode comprising a surface at which an oxidative drug-metabolizing enzyme (DME) is immobilized to allow efficient transfer of electrons from the electrode to a catalytic site within the DME.

34. (New) An electrode according to claim 33, wherein the DME is immobilized to the surface of the electrode by means of a linker.

35. (New) An electrode according to either claim 33 or 34, wherein the DME is covalently immobilized to the surface of the electrode.

36. (New) An electrode according to either claim 33 or 34, wherein the DME is non-covalently immobilized to the surface of the electrode.

37. (New) An electrode according to claim 33, wherein the surface of the electrode is modified by covalent or non covalent addition of chemical groups.

38. (New) An electrode according to claim 37, wherein the electrode is a gold electrode and the chemical groups are organothiolate compounds.

39. (New) An electrode according to either claim 33 or 34, wherein the electrode surface is coated with a mechanically and chemically stable polymer gel having high ionic conductivity, and the DME is trapped within the polymer gel.

40. (New) An electrode according to claim 39, wherein the polymer gel comprises polymers having a high proportion of carboxylic acid groups and the DME has positively-charged surface residues.

41. (New) An electrode according to claim 39, wherein the polymer gel comprises polymers having a high proportion of amine groups and the DME has negative charges at the surface.

42. (New) An electrode according to claim 39, wherein the polymer gel comprises polymers having a high proportion of aliphatic groups and the DME has a hydrophobic surface.

43. (New) An electrode according to either claim 33 or 34, wherein the DME is a cytochrome P450 (CYP) which is by means of a lipid membrane deposited on the surface of the electrode.

44. (New) An electrode according to claim 43, wherein the lipid membrane comprises long-chain fatty acids or lipids.

45. (New) An electrode according to claim 34, wherein the linker comprises a delocalized electron system.

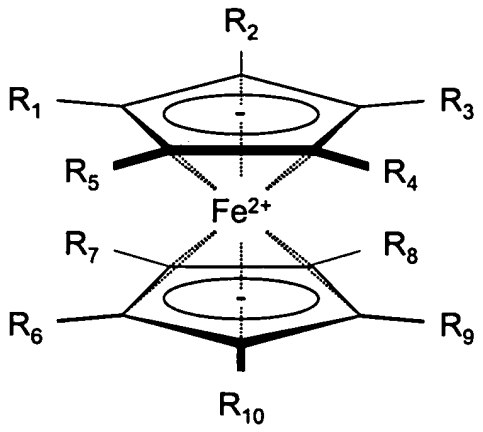
46. (New) An electrode according to claim 34 wherein the linker comprises a functional group that is selected from the group consisting of a hydroxyl

group, an amide, an amine, a carboxylic acid group, an aromatic group, a cyclic group, a heterocyclic group, a thiophene, a nitrogen-containing heterocyclic group, a pyridine, a purine, a pyrimidine, an enol, an ether, a ketone, an aldehyde, a thiol, a thioether, a halo-, a nitro-, a phospho- and a sulphate group.

47. (New) An electrode according to claim 34 wherein the linker comprises a metallocene, a flavin, a quinone, or NADH.

48. (New) An electrode according to claim 47 wherein the linker comprises a metallocene that comprises a ferrocene.

49. (New) An electrode according to claim 48 wherein the ferrocene is a compound of the following formula:



wherein:

R1 is a functional group selected from the group consisting of a thiol, a thioether, an amide, an amine, a carboxylic acid, a heterocyclic group, a thiophene, a nitrogen containing heterocyclic group, a pyridine, a purine and a pyrimidine; and

$R_{2\text{-}10}$ are each independently a functional group selected from the group consisting of a hydroxyl group, an amide, an amine, a carboxylic acid group, an aromatic group, a cyclic group, a heterocyclic group, a thiophene, a nitrogen-containing

heterocyclic group, a pyridine, a purine, a pyrimidine, an enol, an ether, a ketone, an aldehyde, a thiol, a thioether, a halo-, nitro-, phospho-, and a sulphate group.

50. (New) A metal electrode having a surface modified by covalent or non covalent addition of a chemical group to allow transfer of electrons from the electrode to a catalytic site within a solubilized DME at a rate that is at least as fast as a rate of consumption of electrons by the DME when metabolizing a candidate drug.

51. (New) An electrode according to claim 50 wherein the electrode is a gold electrode and the chemical group comprises an organothiolate compound having (i) an SH group which forms a bond to the surface of the electrode, and (ii) a functional group for interacting with the solubilized DME.

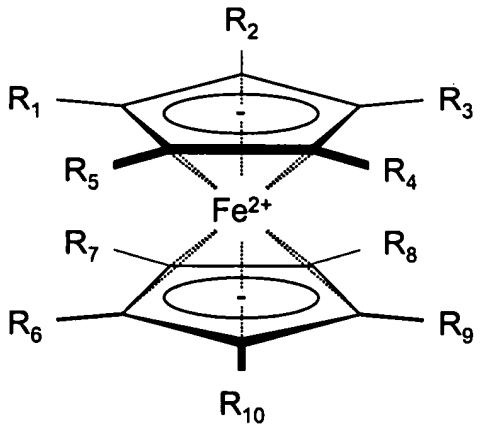
52. (New) An electrode according to claim 51 wherein the chemical group comprises a delocalized electron system.

53. (New) An electrode according to either claim 50 or 52, wherein the chemical group comprises a functional group selected from the group consisting of a hydroxyl group, an amide, an amine, a carboxylic acid group, an aromatic group, a cyclic group, a heterocyclic group, a thiophene, a nitrogen-containing heterocyclic group, a pyridine, a purine, a pyrimidine, an enol, an ether, a ketone, an aldehyde, a thiol, a thioether, a halo-, nitro-, phospho-, and a sulphate group.

54. (New) An electrode according to claim 50 wherein the chemical group comprises a metallocene, a flavin, a quinone, or NADH.

55. (New) An electrode according to claim 54 wherein the chemical group comprises a metallocene that comprises a ferrocene.

56. (New) An electrode according to claim 55, wherein the ferrocene is a compound of the following formula:



wherein:

R1 is a functional group selected from the group consisting of a thiol, a thioether, an amide, an amine, a carboxylic acid, a heterocyclic group, a thiophene, a nitrogen containing heterocyclic group, a pyridine, a purine, and a pyrimidine; and

$R_{2\text{-}10}$ are each independently a functional group selected from the group consisting of a hydroxyl group, an amide, an amine, a carboxylic acid group, an aromatic group, a cyclic group, a heterocyclic group, a thiophene, a nitrogen-containing heterocyclic group, a pyridine, a purine, a pyrimidine, an enol, an ether, a ketone, an aldehyde, a thiol, a thioether, a halo-, nitro-, phospho-, and a sulphate group.

57. (New) An electrochemical reaction chamber comprising a first electrode according to the metal electrode of claim 33; and a second electrode.

58. (New) A device comprising a plurality of electrochemical reaction chambers according to claim 57, wherein the first electrode of each electrochemical reaction chamber comprises a different DME.

59. (New) An electrochemical reaction chamber comprising a first electrode according to the metal electrode of claim 50; a second electrode; and a DME.

60. (New) A device comprising a plurality of electrochemical reaction chambers according to claim 59, wherein the first electrode of each electrochemical reaction chamber comprises a different DME.

61. (New) A method of determining metabolism of a drug by a drug-metabolizing enzyme, comprising:

providing (i) a candidate drug and (ii) a metal electrode that comprises a surface at which an oxidative drug-metabolizing enzyme (DME) is immobilized to allow efficient transfer of electrons from the electrode to a catalytic site within the DME, under conditions that allow transfer of electrons from the electrode to a catalytic site within the DME;

applying changing voltage to the electrode to supply the DME with electrons; and

measuring a rate of consumption of the electrons by the DME, and therefrom determining metabolism of the candidate drug by the DME.

62. (New) A method of determining metabolism of a drug by a drug-metabolizing enzyme, comprising:

providing a candidate drug in solution in an electrochemical reaction chamber, wherein the chamber comprises a metal electrode that comprises a surface at which an oxidative drug-metabolizing enzyme (DME) is immobilized to allow efficient transfer of electrons from the electrode to a catalytic site within the DME, under conditions that allow transfer of electrons from the electrode to a catalytic site within the DME;

applying changing voltage to the electrochemical reaction chamber; and

measuring current flowing through the electrochemical reaction chamber, and therefrom determining metabolism of the candidate drug by the DME.

63. (New) A method of determining metabolism of a drug by a drug-metabolizing enzyme, comprising:

providing (i) a candidate drug and (ii) metal electrode having a surface modified by covalent or non covalent addition of chemical groups to allow transfer of electrons from the electrode to a catalytic site within a solubilized DME at a rate that is at least as fast as a rate of consumption of electrons by the DME when metabolizing a candidate drug;

applying changing voltage to the electrode to supply the DME with electrons; and

measuring a rate of consumption of the electrons by the DME, and therefrom determining metabolism of the candidate drug by the DME.

64. (New) A method of determining metabolism of a drug by a drug-metabolizing enzyme, comprising:

providing a candidate drug in solution in an electrochemical reaction chamber, wherein the chamber comprises a metal electrode having a surface modified by covalent or non covalent addition of chemical groups to allow transfer of electrons from the electrode to a catalytic site within a solubilized DME at a rate that is at least as fast as a rate of consumption of electrons by the DME when metabolizing a candidate drug;

applying changing voltage to the electrochemical reaction chamber; and

measuring current flowing through the electrochemical reaction chamber, and therefrom determining metabolism of the candidate drug by the DME.